Master's Thesis Biophysics/Chemistry • From Jan/Feb 2023

Groups of Jérôme Hénin and Guillaume Stirnemann, CNRS Institut de Biologie Physico-Chimique, Paris, France

Response of a transmembrane protein to high pressures as seen by atomistic simulations

Subject High pressure can be used experimentally to modulate the conformational landscape of proteins, in particular in NMR experiments that can capture the structural and dynamic changes upon changes in pressure. On a broader perspective, understanding the impact of pressure on protein structure and dynamics is important to get a better comprehension of the evolutionary pathways that have led to pressure resistance in some organisms that thrive in extreme pressure conditions.

Preliminary experimental results of our collaborators (E. Lescop, ICSN, and Laurent Catoire, IBPC) suggest that high pressure affects both the local dynamics of the transmembrane protein OmpX and its interactions with lipids. All-atom simulations are the ideal tool to produce a high-resolution description of these phenomena, leading to better physical understanding. The goal of this internship is to use molecular dynamics simulations to model the pressure response (0-2500 bar range) of the transmembrane protein OmpX embedded in a lipid membrane. Both the protein dynamics and the lipid bilayer response will be characterized in detail, and results will be compared with experimental observables, validating the simulation approach in the process.

Techniques/Methods The candidate will gain strong experience in molecular dynamics simulations (no previous experience is required), using a widely-employed and distributed code, as well as advanced techniques to accelerate the sampling of the conformational space of biomolecules. Tools: Molecular dynamics simulations with state-of-the-art RNA forcefields; enhanced sampling methods; programming tools, and simulation analysis tools.

Research environment Research will take place in the lab of Theoretical Biochemistry of the CNRS Institute of Physical and Chemical Biology with Jérôme Hénin and Guillaume Stirnemann. It is located in the very stimulating research environment of the Latin Quarter, at the heart of Paris. Our groups have extensive experience in applying advanced simulation and theoretical tools to tackle a variety of questions, ranging from water ultrafast dynamics in aqueous solutions to the mechanical and thermal stability of proteins. We have access to state-of-the-art computing facilities that include a local mesoscale computer cluster. More information about the lab and the research groups are available here: http://www-lbt.ibpc.fr/people/henin and http://www-lbt.ibpc.fr/people/stirnemann. This internship will take place within a collaboration between a computational and two experimental labs specializing in high-pressure NMR of membrane systems, with frequent interactions between the three project partners.

Extension into a PhD is possible as part of an ANR funding that is already secured for the 2022-2026 period, upon mutual agreement of the candidate and the supervisors.

Contact information Interested candidates should contact Jérôme Hénin (henin@ibpc.fr) and Guillaume Stirnemann **as soon as possible** (stirnemann@ibpc.fr), together with a curriculum vitae and contact information for one or two references.